PATENT
Attorney Docket No.: A-65353-8/RFT/RMS/RMK

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: MAYO, et al.	Examiner: Unknown
	Group Art Unit: 2721
Serial No.: Unknown	"EXPRESS MAIL" MAILING LABEL NUMBER EL659498445US
Filed: Herewith	DATE OF DEPOSIT
For: APPARATUS AND METHOD FOR AUTOMATED PROTEIN DESIGN	I HEREBY CERTIFY THAT THIS PAPER OR FEE IS BEING DEPOSITED WITH THE UNITED STATES POSTAL SERVICE "EXPRESS MAIL POST OFFICE TO ADDRESSEE" SERVICE UNDER 37 CFR 1.10 ON THE DATE INDICATED ABOVE AND IS ADDRESSED TO: BOX PATENT APPLICATION, ASSISTANT COMMISSIONER FOR PATENTS, WASHINGTON, DC 20231.
	TYPED NAME Vincent Diaz
	SIGNED Vincent Diaz

PRELIMINARY AMENDMENT

Assistant Commissioner of Patents
Washington, DC 20231

Sir:

Prior to examination of the above identified application, please amend as follows:

In the Specification:

Please replace the paragraph beginning at page 1, line 2, with the following rewritten paragraph:

--This application claims the benefit of U.S.S.N.s 60/043,464, filed April 11, 1997, 60/054,678, filed August 4, 1997, 60/061,097, filed October 3, 1997, 60/087,561, filed June 1, 1998, and is a continuing application of U.S.S.N. 09/058,459, filed April 10, 1998, now U.S. Patent 6,188,965 and U.S.S.N. 09/714,357, filed November 15, 2000.--

In the Claims:

Please cancel claim 1 without prejudice or disclaimer.

Please add the following claims:

–28. A method executed by a computer under the control of a program, said computer including a memory for storing said program, said method comprising the steps of:

(A) receiving a protein backbone structure with variable residue positions;

(B) establishing a group of potential amino acids for each of said variable residue positions; and

(C) analyzing the interaction of all or part of each of said amino acids with all or part of the remainder of said protein backbone structure to generate a set of optimized protein sequences, wherein said analyzing step includes a Dead-End Elimination (DEE) computation.

29. A method executed by a computer under the control of a program, said computer including a memory for storing said program, said method comprising the steps of:

(A) receiving a protein backbone structure with variable residue positions;

(B) classifying each variable residue position as either a core, surface or boundary residue;

(C) establishing a group of potential amino acids for each of said variable residue positions, wherein the group of potential amino acids for at least one of said variable residue position has an amino acid selected from each of at least two different amino acids; and

(D) analyzing the interaction of all or part of each of said amino acids with all or part of the remainder of said protein to generate a set of optimized protein sequences.

30. A method according to claim 29 wherein said analyzing step comprises a DEE computation.

31. A method according to claim 28 or 29 wherein said set of optimized protein sequences comprises the globally optimal protein sequence.

32. A method according to claim 28 or 30 wherein said DEE computation is selected from the group consisting of original DEE and Goldstein DEE.

33. A method according to claim 28 or 29 wherein said analyzing step includes the use of at least one scoring function.

34. A method according to claim 33 wherein said scoring function is selected from the group consisting of a Van der Waals potential scoring function, a hydrogen bond potential scoring function, an atomic solvation scoring function, an electrostatic scoring function and a secondary structure propensity scoring function.

35. A method according to claim 33 wherein said analyzing step includes the use of at least two scoring functions.

36. A method according to claim 33 wherein said analyzing step includes the use of at least three scoring functions.

37. A method according to claim 33 wherein said analyzing step includes the use of at least four scoring functions.

38. A method according to claim 33 wherein said atomic solvation scoring function includes a scaling factor that compensates for over-counting.

39. A method according to claim 28 or 29 further comprising experimentally testing at least one member of said set.

40. A method according to claim 31 further comprising the step of:

generating a rank ordered list of additional optimal sequences from said globally optimal protein sequence.

41. A method according to claim 40 wherein said generating includes the use of a Monte Carlo search.

42. A method according to claim 29 wherein said analyzing step comprises a Monte Carlo computation.

43. A method according to claim 40 further comprising the step of:

testing some or all of said protein sequences from said ordered list to produce potential energy test results.

44. A method according to claim 43 further comprising the step of:

analyzing the correspondence between said potential energy test results and theoretical potential energy data.

45. A recombinant protein comprising an optimized protein sequence generated by the method of claim 28 or 29.

46. A nucleic acid sequence encoding a recombinant protein according to claim 45.

47. An expression vector comprising the nucleic acid sequence of claim 46.

48. A host cell comprising the nucleic acid sequence of claim 46.

49. A method executed by a computer under the control of a program, said computer including a memory for storing said program, said method comprising the steps of:

(A) receiving a protein backbone structure with variable residue positions;

(B) establishing a group of potential amino acids for each of said variable residue positions, wherein the group of potential amino acids for at least one of said variable residue position has a amino acid selected from each of at least two different amino acids; and

(C) analyzing the interaction of all or part of each of said amino acids with all or part of the remainder of said protein backbone structure to generate a set of optimized protein sequences, wherein said analyzing step includes:

i. a Dead-End Elimination (DEE) computation; and,

ii. at least one scoring function selected from the group consisting of a Van der Waals potential scoring function, a hydrogen bond potential scoring function, an atomic solvation scoring function, an electrostatic scoring function and a secondary structure propensity scoring function.

50. A method executed by a computer under the control of a program, said computer including a memory for storing said program, said method comprising the steps of:

(A) receiving a protein backbone structure with variable residue positions;

(B) classifying each variable residue position as either a core, surface or boundary residue;

(C) establishing a group of potential amino acids for each of said variable residue positions, wherein the group of potential amino acids for at least one of said variable residue position has a amino acid selected from each of at least two different amino acids; and

(D) analyzing the interaction of all or part of each of said amino acids with all or part of the remainder of said protein to generate a set of optimized protein sequences wherein said analyzing step includes:

i. a Dead-End Elimination (DEE) computation; and,

ii. at least one scoring function selected from the group consisting of a Van der Waals potential scoring function, a hydrogen bond potential scoring function, an atomic solvation scoring function, an electrostatic scoring function and a secondary structure propensity scoring function.--

REMARKS

Claim 1 has been cancelled. Claims 28-50 are newly added.

Support for new claims 28-37 and 39-50 is found in original claims 1-20. Support for new claim 38 is found generally on page 16, line 11 through page 18, line 23 and more specifically at page 17, lines 22-33.

The amendment of the paragraph beginning on page 1, line 2 was made to state the relationship of the present application to serial nos. 09/058,459 and 09/714,357.

Attached hereto is a marked-up version of the changes made to the specification and the claims by the preliminary amendment. The attached page is captioned **"Version with markings to show changes made."**

The Commissioner is authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 06-1300 (Our Order No. A-65353-8/RFT/RMS/RMK).

Please direct any calls in connection with this application to the undersigned at (415) 781-1989.

Dated: 4/18/01

Respectfully submitted,

FLEHR, HOHBACH, TEST,
ALBRITTON & HERBERT

By: _____
Renee M Kosslak, Reg. No. 47,717 for
Robin M. Silva Reg. No. 38,304

Four Embarcadero Center - Suite 3400
San Francisco, California 94111-4187
Tel.: (415) 781-1989
Fax: (415) 398-3249
108807.RMK

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the specification:

Paragraph beginning at line 2 of page 1 has been amended as follows:

This application claims the benefit [is a continuing application] of U.S.S.N.s 60/043,464, filed April 11, 1997, 60/054,678, filed August 4, 1997, 60/061,097, filed October 3, 1997, [09/058,459, filed April 10, 1998, and] 60/087,561, filed June 1, 1998, and is a continuing application of U.S.S.N. 09/058,459, filed April 10, 1998, now U.S. Patent 6,188,965 and U.S.S.N. 09/714,357.

In the Claims:

Claim 1 has been canceled.